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Effect of mupirocin on nasal carriage of *Staphylococcus aureus*

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Summary: Mupirocin eliminates nasal carriage of *Staphylococcus aureus* among medical and surgical personnel for periods varying from several weeks up to one year. In persons recolonized after therapy densities of *S. aureus* populations in nares were much lower than in the same persons before therapy.

Keywords: Mupirocin; staphylococcal carriage.

Introduction

The epidemiological importance of nasal carriage of *Staphylococcus aureus* is well recognized. The anterior nares are the main reservoir for this organism from which it may disseminate to the skin or be transmitted from person to person (Williams, 1963). The emergence of methicillin-resistant strains of staphylococci has emphasized the importance of finding methods to treat the carrier state (Ayliffe *et al.*, 1986). Recent reports of nosocomial outbreaks caused by multiple antibiotic-resistant staphylococci have demonstrated that these strains are difficult to eliminate from the hospital environment (Casewell, 1986), since only a small number of colonised personnel are necessary to perpetuate an outbreak.

Several systemic and local antibiotic regimens have been used to eradicate the staphylococcal carrier state (Jarvis & Wigley, 1961; Noble *et al.*, 1964; Martin & White, 1968; Quickel *et al.*, 1971; McAnally, Lewis & Brown, 1984). In most cases, only a temporary suppression was achieved. In other trials the therapy resulted in higher nasal colonisation rates in treated subjects due to suppression of total nasal bacterial flora (Martin & White, 1968).

Mupirocin has been successfully used to eradicate staphylococcal nasal carriage among staff in two separate studies, based upon evaluation of small

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sample groups for a short time (Dacre, Emmerson & Jenner, 1983; Casewell, Hill & Duckworth, 1985). These studies stimulated us to evaluate the efficacy of mupirocin (Bactroban, Beecham, UK) in treating *S. aureus* carriers among hospital personnel over a longer period of time.

Materials and methods

Nasal carriage of *S. aureus* was determined in 348 volunteers among the medical and surgical personnel of our hospital. Carriage categories were estimated according to the formula of Leedom and co-workers (1965), with our own modifications (Heczko *et al.*, 1973) on the basis of the presence of *S. aureus* in six consecutive nasal swabbings taken at weekly intervals. Individuals studied were classified as persistent carriers (PC) when all six cultures were positive for *S. aureus*, or intermittent carriers (IC) when 3–5 cultures showed presence of the bacterium of the same phage and resistance pattern. Transient carriers (TC) differed from IC in harbouring *S. aureus* 3–5 times which were of various phage and/or resistance patterns, while persistent non-carriers (NC) showed all cultures negative for *S. aureus*. The swabs were cultured on Chapman agar (Difco) and on Tryptic Soy Agar (Difco) supplemented with 5% sheep blood for 48 hrs at 37°C. Colonies typical for *S. aureus* were subcultured on blood agar and then tested for production of coagulase by a standard method (Subcommittee on Taxonomy of Staphylococci and Micrococci, 1965). The remaining flora was tested on blood agar and MacConkey agar and then identified using standard methods (Manual of Clinical Microbiology, 1970). Numbers of bacteria on original plates were estimated in a semiquantitative manner by scoring + for 1 to 10 colonies per plate, + + for 10 to 100 colonies and + + + for more than 100 colonies.

Staphylococcus aureus strains were phage typed with phages of the basic set for human strains and experimental phages for Polish *S. aureus* strains (88, 89, 187) (Blair & Williams, 1961; Parker, 1983) and tested for antibiotic resistance by the standard technique of Bauer *et al.* (1966).

The study was conducted in two groups seperately: first, the drug was used in medical staff for five days and its effect followed over one year. The study was then repeated among the surgical staff according to a modified protocol: the drug was given for three days and its effect observed over one month. The study was conducted in a double blind manner; mupirocin was supplied in the form of a sterile nasal ointment, 2% in a paraffin base, together with appropriate placebo. Numbered tubes containing either mupirocin or the placebo were distributed to volunteers according to a randomised code. The volunteers were instructed to apply a small amount of an ointment three times daily to each nostril. Nasal swabs were taken four days after the treatment and then after varying intervals. Post-treatment swabs were cultured as before treatment and strains of *S. aureus* were compared with corresponding strains isolated before the treatment by phage

typing. When phage types were the same before and after treatment, the re-appearance of *S. aureus* was regarded as a relapse; when the types were different, as a reacquisition. In doubtful cases, or when the strains were non-typable, antibiotic resistance patterns were compared.

Results

Sixty nine volunteers classified as persistent, intermittent, or transient carriers of *S. aureus* were treated with mupirocin (Table I). Strains of *S. aureus* isolated before treatment from the medical staff were mostly typed with group II phages (type 3A/3C/55) and more rarely with experimental phages. About 20% were non-typable. Among the strains from surgical staff about 30% were typed as II group and the rest were equally susceptible to the phages of different groups or non-typable.

The drug removed *S. aureus* from nasal swab cultures in all but two volunteers within four days after stopping the treatment (Figure 1). After treatment the percentage of medical staff with positive cultures for *S. aureus* increased and about 30 subjects remained stably colonized during the subsequent six months. 60% of the carriers again yielded *S. aureus* in their nares at one year after treatment, of these 42% showed relapses while 58% were reacquisitions.

Some differences were found between the surgical and medical groups.

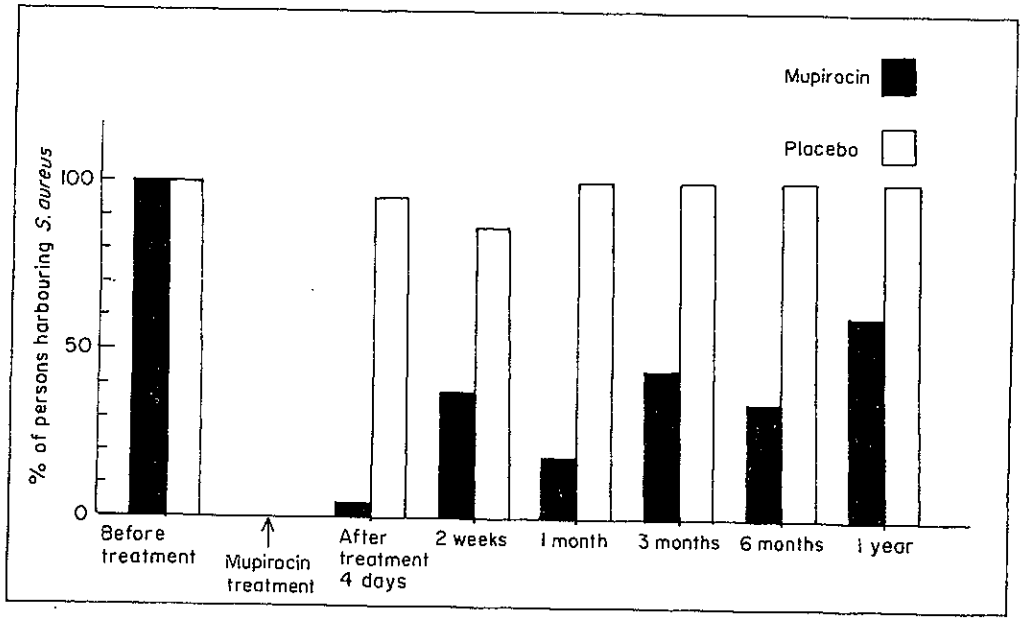

Figure 1. Effect of mupirocin or placebo on nasal carriage of *Staphylococcus aureus* among medical staff.

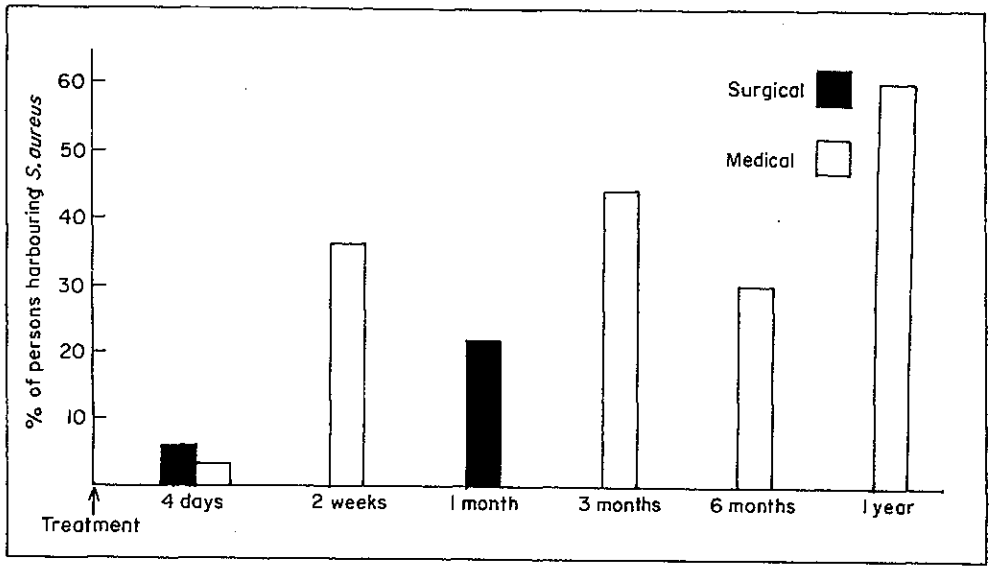

Figure 2. Effect of mupirocin on nasal carriage of *Staphylococcus aureus* in medical and surgical staff.

Only 25% of the surgical personnel returned to carriage of *S. aureus* after one month (Figure 2) while 35% of medical staff yielded *S. aureus* two weeks after stopping mupirocin, with a steady increase to 60% after one year. This difference was explained by comparing the distribution of different carrier categories among the study populations, and by analysing relapses and reacquisitions. Losses of *S. aureus* from nares and relapses occurred mostly among the carriers harbouring strains of II phage group, while reacquisitions occurred among those carrying *S. aureus* of other phage groups or non-typable strains. The reacquired strains were typable with experimental phages. Among eleven persistent carriers from treated medical personnel, relapses were found in four and reacquisitions in six subjects. Among eight intermittent carriers, five persons returned to carriage in one year, two of them reacquired new strains of *S. aureus* while the three others had relapses. On the other hand, the surgical group was composed of persistent, intermittent and transient carriers on more equal proportions (Table II). Only three of them reacquired a new strain of a *S. aureus* while one demonstrated the constant presence of a *S. aureus* strain of the same phage and resistance pattern regardless of treatment. Placebo carriers of the surgical group showed relapses more often than reacquisitions of *S. aureus*.

It was found that mupirocin strongly influenced the density of the *S. aureus* populations in the nares of the treated carriers over a prolonged period (Figure 3). All the subjects selected for this study harboured high numbers of *S. aureus* in their nasal vestibules before treatment, while only a

Table I. *Nasal carriage of* Staphylococcus aureus *among hospital staff volunteers*

Study group	Number (%) of volunteers according to categories of carriage*				Total
	PC	IC	TC	NC	
Medical	28 (15·1)	9 (4·3)	2 (0.9)	169 (79·9)	208 (100)
Surgical	16 (11·4)	4 (2·8)	10 (7·1)	110 (78·7)	140 (100)
Total	44 (12·7)	13 (3·7)	12 (3·4)	279 (80·2)	348 (100)

* PC = persistent carriers; IC = intermittent carriers; TC = transient carriers; NC = persistent non-carriers (see text for definitions).

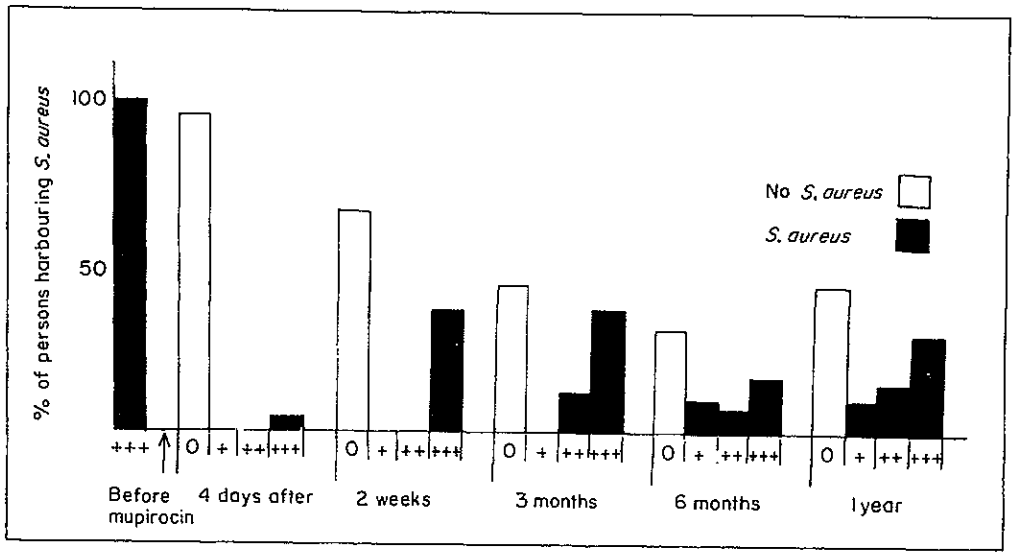

Figure 3. Density of *Staphylococcus aureus* in nasal vestibules of medical staff after mupirocin. + = 1 to 10 colonies of *S. aureus* in primary culture; + + = 11 to 100 colonies; + + + = over 100 colonies.

low proportion showed a comparable density of staphylococcal growth, even one year after treatment.

Discussion

A large number of studies, mostly done about 20 years ago when outbreaks of staphylococcal infection were frequently encountered in hospitals (Williams, 1963), were devoted to the mechanisms of nasal carriage of *S. aureus*. The problem of infections caused by methicillin-resistant staphylococci, which emerged in the latter half of the 1970s and again in the

last decade, has focused the attention of microbiologists on nasal carriage as the reservoir of these organisms (Ayliffe *et al.*, 1986; Casewell, 1986). However, host and parasite factors determining staphylococcal carriage are poorly understood, and it is possible that genetic factors play a role (Aly & Maibach, 1974; Kinsman, McKenna & Noble, 1983).

Up until recently, only two ways of eliminating carriage could be applied with some effect: inhibition of *S. aureus* multiplication in the nares with antibiotics or selective enzymes (Jarvis & Wigley, 1961; Noble *et al.*, 1964; Martin & White, 1968; Quickel *et al.*, 1971; McAnally, Lewis & Brown, 1984), or replacement of epidemic strains of *S. aureus* in the nares with those of presumptive low virulence (Shinefield *et al.*, 1974). Both approaches possess several limitations: antibiotics may cause disappearance of *S. aureus* for only a short period of time, and moreover usually destroy the normal flora of the nasal vestibule, while replacement therapy with *S. aureus* strain 502A may lead to infection induced by this strain.

In our study mupirocin eliminated nasal carriage of *S. aureus* for at least several weeks, a period of time longer than previously reported (Dacre, Emmerson & Jenner, 1983; Casewell, Hill & Duckworth, 1985). We have not found any strain resistant to mupirocin either before or during the study. Although we have not presented the data here, we noted that mupirocin selectively influenced the bacterial populations in the nares. Coagulase-negative staphylococci and diphtheroids were unchanged in number. This is of interest, since Sutherland *et al.* (1985) reported the MIC values of mupirocin for coagulase-negative staphylococci to be similar as those for *S. aureus*.

Table II. *Influence of mupirocin or placebo on* Staphylococcus aureus *nasal carriage in medical and surgical staff*

Carrier type	Loss of *S. aureus*	No change of *S. aureus*	Acquisition of Different Phage Types Strain		Total
	M(S)*	M(S)	M(S)	M(S)	M(S)
Mupirocin					
PC	11(5)	4(0)	5(1)	1(0)	21(6)
IC	3(3)	3(0)	1(0)	1(0)	8(3)
TC	0(4)	0(1)	1(2)	0(0)	1(7)
Placebo					
PC	0(0)	3(7)	4(3)	0(0)	7(10)
IC	0(0)	0(1)	1(0)	0(0)	1(1)
TC	0(0)	1(2)	0(1)	0(1)	1(3)
Total	14(12)	11(11)	12(7)	2(0)	39(30)

* M(S)=Medical (Surgery) staff.

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References

Aly, R. & Maibach, H. I. (1974). *Staphylococcus aureus* carriage in twins. *American Journal of Diseases of Childhood* **127** 468–488.

Ayliffe, G., *et al.* (1986). Guidelines for the control of epidemic methicillin-resistant *Staphylococcus aureus*. *Journal of Hospital Infection* **7**, 193–201.

Bauer, A. W., Kirby, W. M. M., Sherris, J. C. & Turck, M. (1966). Antibiotic susceptibility testing by a standarized single disk method. *American Journal of Clinical Pathology* **45**, 493–496.

Blair, J. E., Williams, R. E. O. (1961). Phage typing of staphylococci. *Bulletin of WHO* **24**, 771–784.

Casewell, M. W. (1986) Epidemiology and control of the 'modern' methicillin-resistant *Staphylococcus aureus*. *Journal of Hospital Infection* **7** (Supl. A), 1–11.

Casewell, M. W., Hill, R. L. R. & Duckworth, G. J. (1985). The effect of mupirocin (pseudomonic acid) on the nasal carriage of *Staphylococcus aureus*. *Excerpta Medica Current Clinical Practice and Serology* **16**, 47–53.

Dacre, J. E., Emmerson, A. M. & Jenner, E. A. (1983), Nasal carriage of gentamicin and methicillin-resistant *Staphylococcus aureus* treated with topical pseudomonic acid. *Lancet* **ii**, 1036.

Heczko, P. B., Pryjma, J., Kasprowicz, A. & Krawiec, H. (1973). Influence of host and parasite factors on the nasal carriage of staphylococci. In *Staphylococci and staphylococcal infections*, (Jeljaszewicz, J. ed.), Vol. 2, pp. 581–594. Basel: Kerger.

Jarvis, A. W. & Wigley, R. D. (1961). Recurrence of staphylocci of the same phage type following control of nasal carriers with neobactrim and soframycin. *Lancet* **ii**. 1168–1170.

Kinsman, O. S., McKenna, R. & Noble, W. C. (1983), Association between histocompatibility antigens (HLA) and nasal carriage of *Staphylococcus aureus*. *Journal of Medical Microbiology* **16**, 215-220.

Leedom, J. M., Kennedy, R. P., Lepper, M. H. & Jackson G. C. (1965). Observations of the staphylococcal nasal carrier state. *Annals of the New York Academy of Sciences* **128**, 381–403.

Manual of Clinical Microbiology, (1970). (Blair, J. E., Lennette, E. H. & Truant, J. P., eds) American Society for Microbiology. Bethesda.

Martin, R. R. & White, A. (1968). The reacquisition of staphylococci by treated carriers: a demonstration of bacterial interference. *Journal of Laboratory and Clinical Medicine* **71**, 791–797.

McAnally, T. P., Lewis, M. R. & Brown D. R. (1984), Effect of rifampin and bacitracin on nasal carriers of *Staphylococcus aureus*. *Antimicrobial Agents and Chemotherapy* **25**, 422–425.

Noble, W. C., Williams R. E. O., Jevons, M. P. & Shooter, R. A. (1964). Some aspects of nasal carriage of staphylococci. *Journal of Clinical Pathology* **17**, 79–83.

Parker, M. T. (1983) The significance of phage-typing patterns in *Staphylococcus aureus*. *In Staphylococci and Staphylococcal infections*. (Easmon, C. S. F., & Adlam, C., eds), Vol. 2, pp 33–62. London: Academic Press.

Quickel, K. E., Selden R., Caldwell, J. R., Nora, N. F. & Schaffner, W. (1971). Efficacy and safety of topical lysostaphin treatment of persistent nasal carriage of *Staphylococcus aureus*. *Applied Microbiology* **22**, 446–450.

Shinefield, H. R., Ribble, J. C., Boris, M., Eichenwald, H. F., Aly, R. & Maibach, H. (1974). Bacterial interference between strains of *S. aureus*. *Annals of the New York Academy of Sciences* **236**, 444–455.

Subcommittee on Taxonomy of Staphylococci and Micrococci (1965) Recommendations. *International Bulletin of Microbiology. Nomenclature & Taxonomy* **15**, 109–110.

Sutherland, R., Boon, R. J., Griffin, K. E., Masters, P. J., Slocombe, B. & White, A. R. (1985). Antibacterial activity of mupirocin (Pseudomonic acid), a new antibiotic for topical use. *Antimicrobial Agents and Chemotherapy* **27**, 495-498.

Williams, R. E. O. (1963). Healthy carriage of *Staphylococcus aureus*: its prevalence and importance. *Bacteriologic Revue* **27**, 56–71.